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09/913,752	11/21/2001	Darja Fercej Temeljotov	104101.B700017	5309

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EXAMINER	
PURDY, KYLE A	
ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/913,752	FERCEJ TEMELJOTOV ET AL.	
	Examiner	Art Unit	
	Kyle Purdy	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71,72,76-82 and 84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71,72,76-82 and 84* is/are rejected.

7)☒ Claim(s) *71 and 84* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the arguments filed on 3/11/2010.

2. Claims 71, 72, 76-82 and 84 are presented for examination on the merits. The following rejections are made.

Claim Objections

3. Claims 71 and 84 are objected to because of the following informalities: claims 71 and 84 are composition claims which depend from method claims. Either 1) the claims from which these depend should be changed or 2) the matter of the claim should be adjusted, i.e. formulation to method. Appropriate correction is required.

Response to Applicants' Arguments

4. Applicants arguments filed 3/11/2010 regarding the rejection of claims 71, 72, 76-82 and 84 made by the Examiner under 35 USC 103(a) over Akiyama et al. (WO 98/42311) in view of Al-Raxxak et al. (US 6010718) have been fully considered but they are not found persuasive.

5. The rejection of claims 71, 72, 76-82 and 84 made by the examiner under 35 USC 103(a) is **MAINTAINED** for the reasons of record in the office action mailed on 12/15/2009.

6. In regards to the 103(a) rejection, Applicant asserts the following:

A) The Examiner has erroneously equated 'obvious to try' with obviousness under 103 because the courts have stated that throwing 'metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness' and that 'to explore' where the prior art gives only 'general guidance' results in impermissible 'obvious to try'. Akiyama teaches broad genera of compounds with broad genera

of weight percentages. Akiyama provides a general teaching, but fails to provide Applicants particular form and how to achieve it; and

B) Al-Razzak does not remedy the deficiencies of Akiyama.

7. In response to A, Akiyama is directed to a gastrointestinal mucosa-adherent pharmaceutical composition which generically comprises a matrix of 1) an active agent; 2) a polyglycerol fatty acid ester; and 3) a viscogenic agent. While these groups themselves are extremely broad, Akiyama goes on to teach/suggest particular agents and amounts of those agents to be employed. With respect to the active agent, Akiyama suggests an active agent being that of a macrolide antibiotic such as clarithromycin. While no specific amount is taught for this specific agent, other prior art references (e.g. Al-Razzak) teach sustained release compositions having 500 mgs of clarithromycin to treat microbial infection (motivation). With respect to the inclusion of a polyglycerol fatty acid ester, this is obvious in view of Akiyama alone. Akiyama teaches Applicants glyceryl behenate, and suggests that it be included in the composition in an amount of from about 5-98% by weight, preferably about **20**-95% by weight, and more preferably from 40-95% by weight (see column 7, lines 25-30). Not only does Akiyama provide a range which entirely encompasses Applicants range, Akiyama provides a percentage weight which directly reads on Applicants claimed range. If the art recognizes that a polyglycerol fatty acid ester can be used for a general purpose (e.g. glyceryl behenate) within a specific range or at given value, then any person would have had a reasonable expectation for success in their product/method, which uses a value within that range, being suitable for use in the field of endeavor of the prior art. With respect to the inclusion the viscogenic agent, Akiyama suggests

hydropropylmethylcellulose (HPMC). The amount of viscogenic agent is taught at column 10, lines 5-10:

> 'Referring to the amount of the viscogenic agent for use in the composition of the invention, its amount in the gastrointestinal mucosa-adherent matrix may for example be about 0.005 to about 99 weight %, preferably about 0.5 to about 45 weight %, more preferably about 1 to about 30 weight %, furthermore preferably about 1 to about 25 weight %, and for still better result, about 1 to about 20 weight %.'

Thus, contrary to Applicants arguments, while Akiyama does provide a very broad range for the viscogenic agent (0.005-99%), it's taught that for the best results an amount from between 1-20% is to be used. Thus the Examiner contends that Akiyama as a whole is not equivalent to 'throwing metaphorical darts at a board filled with combinatorial prior art possibilities'. Rather, because Akiyama provides a general structure and preferred narrow means for achieving that structure, any ordinary person would have been capable of selecting and included Applicants claimed agents. Thus, their selection and inclusion would have been 'obvious to try'. Applicants arguments are not persuasive.

8. In response to B, while Akiymam teaches component weight percentages, Akiyama fails to teach including them in 'mg' amounts. Al-Razzak was cited to illustrate that Applicants claimed amount of HPMC and clarithromycin were known at the time the invention was made, and they would have been obvious to supplement in the teaching of Akiyama. Applicants argument is not persuasive.

Maintained Rejections, of Record
Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. **Claims 71, 72, 76-82 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akiyama et al. (WO 98/42311; of record) in view of Al-Razzak et al. (US 6010718; field 04/11/1997).**

12. Akiyama teaches a gastrointestinal mucosa adherent matrix adapted to stay long in the gastrointestinal tract for sustained drug release. The gastrointestinal mucosa-adherent matrix which is solid at ambient temperature includes a matrix in which each matrix particle containing a polyglycerol fatty acid ester and/or a lipid and an active ingredient has a coating layer comprising or containing the viscogenic agent.

13. Examples of viscogenic agent include polymers containing carboxyl groups or salts thereof, cellulose ethers, polyethylene glycols having molecular weights not less than 200,000, and naturally-occurring mucous substances. The preferable viscogenic agents are those having a viscosity in the range of 3 to 50,000 cps, preferably 10 to 30,000 cps, and more preferably 15 to 30,000 cps as a 2 percent by weight aqueous solution thereof at 20.degree. C. Cellulose ethers taught include hydroxymethylcellulose and hydroxypropylmethylcellulose (HPMC) (see page

17, lines 10-35 and page 18, line 36). The viscogneic agent is taught in a preferable amount of 1-20% (see page 19, lines 10-15).

14. The matrix may also comprise a polyglycerol fatty acid ester. The polyglycerol fatty acid esters includes behenyl glycerides and the lipids include glycerol fatty acid esters wherein behenic acid is taught as a fatty acid (see page 8, lines 1-5, page 10, and page 12, lines 8-36). The lipid is utilized in an amount of 5-98%.

15. The active includes antimicrobial substance and preferably clarithromycin. See page 14, lines 25-30 and page 15, lines 1-2. The active is used in an amount of 0.005-95% and preferably about 10 to about 50% (see page 26, lines 12-20).

16. The solid composition may be coated with a coating material including hydroxypropylmethylcellulose phthalate (see page 22, lines 15-25 and page 23, lines 30-35). The solid dosage form includes tablets (see page 25, line 14). The composition includes surfactants (see page 29, lines 1-15).

17. Akiyama does not teach the clarithromycin being present in the tablet in an amount of 500 mgs nor does Akiyama teach including HPMc in an amount of 150 mgs.

18. Al-Razzark is directed to extended release formulation of erythromycin derivatives. Example 1 teaches using clarithromycin in an amount of 500 mgs and low-viscosity HPMC in amounts of 100, 200 and 300 mgs. It's indicated that this amount of clarithromycin is useful for the treatment of microbial infections (see column 3, lines 40-45).

19. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Akiyama and Al-Razzak to arrive at a

composition comprising glycerol behenate and 500 mgs of clarithromycin. As Akiyama teaches that clarithromycin may be delivered by the tablet, any ordinary person would have looked to the art for suitable amounts of clarithromycin for delivering to a subject. If such an undertaking resulted in the identification of 500 mgs, as Al-Razzak teaches, then such would have been the result of ordinary skill and common sense. Including such an amount of clarithromycin would have been obvious as Al-Razzak suggests that 500 mgs is suitable for the prophylaxis to microbial infections. With respect to the amount of HPMC (weight percent and mg amount), this is obvious as Akiyama incorporates viscogenic agent is incorporated preferably amount of the viscogenic agent is 1-20%, which encompasses Applicants "about 13-18 weight percent". Moreover, Al-Razzak teaches tablets comprising 100, 200 and 300 mgs of HPMC which provide sustained release benefit. It would have been readily apparent to any ordinary person to pick and choose from values within these ranges, i.e. 150 mgs with a reasonable expectation that that value too would provide a sustained release benefit. With respect to the inclusion of glyceryl behenate, this is also obvious as it is suggested by Akiyama to be used in an amount of 5-98% of the tablet weight. One would have been motivated to include glyceryl behenate as it's known to provide sustained release properties. With respect to the concentration (weight percent and mg amount) of glyceryl behenate, it would have been well within the skill of an artisan to manipulate the concentration and mg amount based on the general disclosure provided by the prior art absent evidence of the unexpectedness of the claimed range. It's noted that the taught range by Akiyama encompasses the instantly claimed range, as such, the mg amount would necessarily stem from knowing/having a final target tablet weight. Therefore, the invention as a whole is *prima facie*

obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

Conclusion

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

21. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

23. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

24. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Kyle Purdy/
Examiner, Art Unit 1611
May 26, 2010

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611